REMARKS

Claims 1-20 are currently pending in the application. Claims 3-6 and 8-20 have been canceled without prejudice. Claims 1, 2 and 7 have been amended. A marked-up version illustrating the claim amendments is annexed hereto. New claims 21-29 have been added, but no new matter has been introduced by virtue of the new claims. Applicant respectfully requests reconsideration of the claim rejections based on the above amendments and the following remarks.

Election/Restriction Requirement

Although Applicant respectfully disagrees with the restriction requirement, claims 8-20 have been canceled without prejudice as being withdrawn from consideration.

Claim Rejections - 35 U.S.C. § 112

Claims 1-7 were rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth on pages 2-6 of the Office Action. The specific rejection of claims 3-6 is moot since such claims have been canceled without prejudice. Applicant respectfully submits that at the very minimum, claims 1, 24 and 27 satisfy the requirements of 35 U.S.C. § 112, first paragraph.

Claims 1, 24 and 27 are directed to methods for determining if a person has, or can develop, PDD, Parkinson's disease or a Dysautonomic disorder. The methods comprise the steps of analyzing a stool sample of an individual to determine the presence of antigens associated with a plurality of different pathogens. The presence of a plurality of different antigens in the stool sample indicates that the individual either has, or can develop, such disorders.

Applicant has submitted herewith a Declaration under 37 C.F.R. 1.132 (the "Declaration") presenting statistical analyses to demonstrate that data presented in the Applicant's specification is sufficient to establish the existence of a "reasonable correlation" between the presence of a plurality of different antigens in a stool sample of an individual and the individual either having a disorder such as Dysautonomia, Parkinson's disease, and PDD (such as Autism, ADD and ADHD), or the potential for the individual to develop such disorders.

To the extent that Examiner challenges the utility of Applicant's claimed inventions, it respectfully submitted that evidence produced by Applicant will be sufficient if, considered as a whole, it leads a person of ordinary skill in the art to conclude that the asserted utility is more likely than not true (see MPEP 2107.02 (VII)). Further, all that is required is that a *reasonable correlation* exists between the activity and asserted use and Applicant is not required to establish utility "as a matter of statistical certainty." (See MPEP 2107.03 (I)).

It is respectfully submitted that the existence of a "reasonable correlation" between the presence of a plurality of different antigens in a stool sample of an individual and the individual either having a disorder such as Dysautonomia, Parkinson's disease, and PDD (such as Autism, ADD and ADHD), or the potential for the individual to develop such disorders, is demonstrated by the following:

(i) Applicant's specification is replete with disclosure and experimental data that demonstrates, for example, that *common links exist* between disorders such as Parkinson's disease, PDD and Dysautonomia *vis-à-vis* GI function (e.g., the presence of multiple pathogens, low fecal chymotrypsin levels) and that the presence of multiple pathogens in the stool is

characteristic of individuals having PDD, Parkinson's disease or Dysautonomia. Indeed, by way of example, experimental Case 1 (Fig.1) demonstrates that individuals with Familial Dysautonomia have multiple pathogens present in their stools, experimental Case 2 (Fig. 2) demonstrates individuals with Parkinson's disease have multiple pathogens present in their stools, as compared to non-Parkinson's individuals, experimental case 3 (Fig. 3) demonstrates individuals with ADD orADHD have multiple pathogens present in their stools, as compared to non-ADD or ADHD individuals, and experimental Case 4 (Fig. 4) demonstrates that Autistic individuals have multiple pathogens present in their stools; and

(iii) the statistical analyses presented in Applicant's Declaration demonstrate at the very minimum that reasonable correlations exist between the presence of a plurality of different antigens in a stool sample of an individual and the individual either having a disorder such as Dysautonomia, Parkinson's disease, and PDD (such as Autism, ADD and ADHD), or the potential for the individual to develop such disorders.

Applicant respectfully submits that at the very minimum, claims 1, 24 and 27 are enabled by the teachings of Applicant's specification. With respect to enablement under 35 U.S.C. § 112, the invention that must be enabled in that defined by the particular claims of the patent application (MPEP 2164). An analysis of whether a given claim is supported by Applicant's specification is whether one reasonably skilled in the art could make or use the invention from Applicant's specification, coupled with information known in the art, without *undue experimentation* The determination of what constitutes undue experimentation is based on a standard of reasonableness with regard to the nature of the invention and the state of the art. The

test of enablement is not quantitative, since a considerable amount of experimentation is permissible if merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed (MPEP 2164.06). Indeed, enablement should be found with respect to a claimed invention when there is reasonable direction and guidance in the specification and all the methods needed to practice the invention are well-known (see, MPEP 2164.01).

Here, with respect to the claimed inventions, various tests, procedures and assays for detecting antigens of various pathogens are well known in the art. Furthermore, various tests, tools and diagnostic criteria are well-known in the art for diagnosing and evaluating PDD, Dysautonomia and Parkinson's disease. Therefore, in view of the fact that various methods for detecting antigens in the stool and for diagnosing and analyzing such disorders are known to those of ordinary skill in the art, and given the amount of direction provided by Applicant with respect to the various types of pathogens found in the stools of individuals with such disorders, Applicant respectfully submits that undue experimentation would not needed to practice the inventions of claims 1, 24 and 27. Indeed, even assuming, *arguendo,* that extensive experimentation may be needed to enable one to regularly use the presence of multiple pathogens as a biomarker for such disorders at predictability levels suggested by Examiner, it is submitted that such experimentation would not be *undue*.

Therefore, based on the above, the withdrawal of the claim rejections under 35 U.S.C. §112, first paragraph, is respectfully requested.

Claim Rejections - 35 U.S.C. § 102

The following claim rejections were made under 35 U.S.C. § 102(b):

(i) claims 1 and 2 were rejected as being anticipated by Parisi et al, Journal of Clinical Microbiology, Vol. 33, pp 1963-1965 ("Parisi");

(ii) claims 1 and 2 were rejected as being anticipated by U.S. Patent No. 5,607,863 to Chandler ("Chandler");

(iii) claim 7 was rejected as being anticipated by Chandler;

(iv) claims 1, 2 and 7 were rejected as being anticipated by U.S. Patent No. 5,527,678 to Blaser et al ("Blaser");

(v) claim 1 was rejected as being anticipated by U.S. Patent No. 5,952,178 to Lapidus et al ("Lapidus"); and

(vi) claim 4 was rejected as being anticipated by Woodward, et al., "Ischameic enterocolitis complication idiopathic dysautonomia", Gut 1998; 43:285-287 ("Woodward").

The above rejections are believed to be moot in view of the claim amendments and additions. However, it is respectfully submitted that at the very minimum, claims 1, 24 and 27 are believed to be patentably distinct and patentable over Parisi, Chandler, Blaser, Lapidus, and Woodward since non of the cited references discloses or suggests *identifying the presence of a plurality of different antigens in a stool sample as a biomarker that indicates that the individual either has, or can develop, PDD, Parkinson's disease or a dysautonomic disorder,* as essentially claimed in claims 1, 24 and 27, respectively.

Indeed, although Parisi teaches an immunoassay for detecting the presence of cyptosporidium in the stool, there is nothing in Parisi that discloses or suggests *identifying the presence of a plurality of different antigens in a stool sample as a biomarker that indicates that the individual either has, or can develop, PDD, Parkinson's disease or a dysautonomic disorder,* as essentially claimed in claims 1, 24 and 27, respectively.

Further, Chandler discloses an assay device that can perform various immunoassays to detect analytes of biological interest, such as antigens specific to pathogens and testing fecal samples to detect fecal occult blood, etc. However, there is nothing in Chandler that discloses or suggests *identifying the presence of a plurality of different antigens in a stool sample as a biomarker that indicates that the individual either has, or can develop, PDD, Parkinson's disease or a dysautonomic disorder,* as essentially claimed in claims 1, 24 and 27, respectively.

In addition, although Blaser is related to methods for detecting for the presence of H. pylori infection to diagnose certain diseases, Blaser does not disclose or suggest *identifying the presence of a plurality of different antigens in a stool sample as a biomarker that indicates that the individual either has, or can develop, PDD, Parkinson's disease or a dysautonomic disorder,* as essentially claimed in claims 1, 24 and 27, respectively.

Moreover, although Lapidus discloses a method for diagnosing disease from stool samples, such methods include detecting in a stool sample the presence of cells or cellular debris that are shed from epithelial cells lining the colon that may be indicative of cancer or precancer (col. 2, lines 31-35). There is nothing in Lapidus that remotely relates to testing for the presence of a pathogen in the stool, much less *identifying the presence of a plurality of different antigens*

in a stool sample as a biomarker that indicates that the individual either has, or can develop, PDD, Parkinson's disease or a dysautonomic disorder, as essentially claimed in claims 1, 24 and 27, respectively.

Finally, although Woodward discloses that stool samples of an individual that suffered a dysautonomic condition were tested for Clostridium difficile, Woodward repeatedly found the stool samples of the individual to be negative for such pathogen (see, page 285). Thus, it is abundantly clear that there is nothing in Woodward that remotely discloses or suggests *identifying the presence of a plurality of different antigens in a stool sample as a biomarker that indicates that the individual either has, or can develop, PDD, Parkinson's disease or a dysautonomic disorder,* as essentially claimed in claims 1, 24 and 27, respectively.

Thus, for at least the above reasons, claims 1, 24 and 27 (and all claims that depend therefrom) are patentably distinct and patentable over Parisi, Chandler, Blaser, Lapidus, and Woodward. Accordingly, the withdrawal of the claim rejections under 35 U.S.C. 102 is respectfully requested.

Claim Rejections - 35 U.S.C. § 103

Claims 5 and 7 were rejected under 35 U.S.C. § 103 as being unpatentable over either Parisi or Chandler in view of Dobbs et al, Medical Hypothesis, vol. 55, pp 93-98 ("Dobbs"). Claim 5 has been cancelled without prejudice and the specific rejection is thus moot. Furthermore, the combination of Parisi, Chandler and Dobbs is legally deficient to establish a *prima facie* case of obviousness against claim 7 because such combination does not disclose or suggest *identifying the presence of a plurality of different antigens in a stool sample as a*

biomarker that indicates that the individual either has, or can develop, PDD, wherein at least one of the plurality of different pathogens is Helicobacter pylori, as essentially claimed in claim 7.

Furthermore, the combination of Parisi, Chandler and Dobbs would be legally deficient to establish a *prima facie* case of obviousness against new claim 24 because such combination does not disclose or suggest *identifying the presence of a plurality of different antigens in the stool sample as a biomarker that indicates that the individual either has Parkinson's disease or can develop Parkinson's disease.* Indeed, although Dobbs arguably discloses a weak link between H pylori infection and idiopathic parkinsonism, Dobbs merely teaches the existence of infection of a *single* pathogen, H. pylori, but not *a plurality of antigens in a stool sample as a biomarker* for a Parkinson's disease, as essentially claimed in claim 24.

Claims 1, 6 and 7 were rejected under 35 U.S.C. § 103 as being unpatentable over Blaser as applied to claim 1, in view of Tsang, et al, Hong Kong Medical Journal, Vol. 5, pp 169-174 ("Tsang"). Claim 6 has been canceled without prejudice and the specific rejection is thus moot. The combination of Blaser and Tsang is legally deficient to establish a *prima facie* case of obviousness against claims 1 and 7 because such combination does not disclose or suggest *identifying the presence of a plurality of different antigens in a stool sample as a biomarker that indicates that the individual either has, or can develop, PDD*, as essentially claimed in claim 1, and further *wherein at least one of the plurality of different pathogens is Helicobacter pylori*, as essentially claimed in claim 7. Indeed, although Tsang discloses a plurality of diseases thought

to be associated with H. pylori infection, Tsang does not teach or suggest that PDD is associated with multiple pathogen infection including H. pylori infection.

Claims 3 and 7 were rejected under 35 U.S.C. § 103 as being unpatentable over Blaser in view of U.S. Patent No. 6,020,310 to Beck et al. ("Beck"). Claim 3 has been canceled without prejudice and the specific rejection is thus moot. The combination of Blaser and Beck is legally deficient to establish a *prima facie* case of obviousness against claim 7 because such combination does not disclose or suggest *identifying the presence of a plurality of different antigens in a stool sample as a biomarker that indicates that the individual either has, or can develop, PDD, wherein at least one of the plurality of different pathogens is Helicobacter pylori*, as essentially claimed in claim 7. Indeed, although Beck discloses that biopsies were preformed to detect the presence of H. pylori in Autistic children, Beck never discloses a positive finding of the presence of H. pylori, much less detecting multiple antigens in a stool sample as an indicator of PDD. In fact, Beck discloses that the duodenal fluid specimens of 11 children were tested for bacteria and fungi and the tests were all normal (see, Col. 17, lines 1-4). As such, Applicant respectfully disagrees with the contention that Beck "teaches a correlation between the pathogen H. pylori and autism", as asserted on page 11 of the office Action. In contrast, Beck teaches away from the proposed combination because Beck's finding with respect to pathogens was negative.

For at least all of the above reasons, the withdrawal of the claim rejections under 35 U.S.C. 103(a) is respectfully requested.

In view of the foregoing remarks and amendments, it is respectfully submitted that all the claims now pending in the application are in condition for allowance. Early and favorable reconsideration of the case is respectfully requested.

Respectfully submitted,

Frank V. DeRosa
Reg. No. 43, 584
Attorney for Applicant

F. Chau & Associates, LLP
1900 Hempstead Tnpk.
East Meadow, NY 11553
TEL.: (516) 357-0091
FAX: (516) 357-0092

Marked-Up Version Illustrating Claim Amendments

1. (Amended) A method for determining if a person has, or can develop, a PDD (pervasive development disorder) [disorder or condition], comprising the steps of:

obtaining a stool sample from the individual;

analyzing the stool sample to determine the presence of antigens associated with a plurality of different pathogens; and

[correlating the presence of the pathogen with a disorder or lack thereof] identifying the presence of a plurality of different antigens in the stool sample as a biomarker that indicates that the individual either has a PDD or can develop a PDD.

2. (Amended) The method of claim 1, wherein the step of analyzing comprises performing a stool immunoassay [to determine the presence of an antigen associated with a pathogen].

7. (Amended) The method of claim 1, wherein at least one of the plurality of different pathogens [comprises] is Helicobacter pylori.